

CASE STUDY

GLIOBLASTOMA MIMICKING AN ABSCESS: A RADIO-PATHOLOGICAL CASE REPORT

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ABSTRACT: Glioblastoma is an aggressive malignant glial neoplasm of the CNS with a dismal prognosis. It often presents as a ring enhancing lesion on imaging and if accompanied by abundant necrosis, it can often be misinterpreted as an abscess. Even on a histological examination, in the background of predominantly necrosis, the neoplasm might be missed without a thorough evaluation. This case had a similar presentation accompanied by an exuberant granulation tissue response mimicking an abscess, however no organism was found. A detailed radiological, pathological and microbiological evaluation is presented.

KEYWORDS: Glioblastoma; Abscess; Necrosis; Ring enhancing.

INTRODUCTION:

Glioblastoma (GBM) is the most common primary malignant glial neoplasm of the central nervous system. It is a WHO grade IV tumor in the 2016 WHO classification of tumors of central nervous system (CNS). Traditionally, it was known as glioblastoma multiforme, owing to its varied radiological and histological picture. But the hallmarks remain microvascular proliferations and necrosis. This necrosis assumes either a palisading configuration and/or as vast swathes of confluent necrosis. Rarely, this confluent necrosis is so overwhelming in the morphological picture that it obscures the underlying neoplasm and can lead to misinterpretation of diagnosis. We present one such case which presented us a unique diagnostic dilemma.

CASE REPORT:

A 65-year-old gentleman presented with a short history of headache lasting 15 days and recently worsened along with loss of appetite and an altered sensorium for the past 3 days. There was no history of loss of consciousness, fever or seizures. His Glasgow Coma Scale (GCS) score was E4M5V2. Pupils were equal and reactive to light. He had a right upper limb paralysis. CT scan showed a contrast ring enhancing solid/cystic lesion 4.5 x 4.7cm in dimensions in the left parietal lobe with a mass effect and midline shift (Figure 1A). The radiological differential diagnoses were abscess or a neoplasm (glioma/metastasis). His routine blood counts, liver function tests, renal function tests and serum electrolytes were within normal range. CSF analysis showed markedly elevated proteins. Gram's stain of

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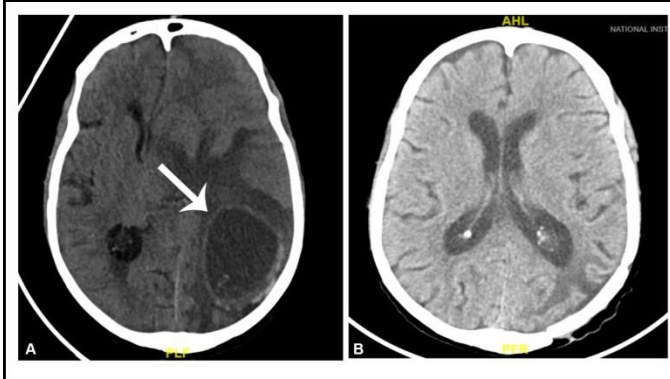


Figure 1. Computed tomography scan showing a ring enhancing lesion (A, arrow) with central area of necrosis in left parietal lobe. Post-operative scan showing near total excision of lesion with compensatory ventriculomegaly of left occipital horn (B).

CSF showed no bacteria and culture showed no growth. No other co-morbidities or immuno-compromising factors were found. No other systemic complaints pointing towards a primary malignancy was found on clinical examination. Decompressive surgery was performed and the excised lesion was sent for histopathology. Post-operative course was uneventful.

predominantly necrosis (C, asterix) and an abscess wall composed of granulation tissue response (C, hash) with small islands of neoplastic glial cells (D, arrow). [Hematoxylin and eosin stain, magnifications of 40X, 100X and 200X in B, C, D respectively] Immunohistochemistry showing the neoplastic glial cells with GFAP positivity (E, immunoperoxidase, 100X) and cytokeratin negativity (F, immunoperoxidase, 200X).

The specimen was cut open and showed a large necrotic cystic cavity exuding copious amount of pus which was sent for culture and sensitivity analysis (Figure 2A). Specimen was fixed routinely in 10% neutral buffered formalin for 24 hours and routine sections were taken (4-5µm) for hematoxylin and eosin staining. The sections showed an organizing abscess wall replete with large central necrotic and karryorhectic zone which was rimmed by a brisk granulation tissue response. This response was composed of a palisading rim of proliferating fibroblasts, neo-angiogenesis and a mixed inflammatory cell infiltrate of neutrophils, lymphocytes and macrophages. Bordering this zone of granulation tissue, there were syncytial islands of neoplastic cells with an irregular nuclear outline and having ample amount of eosinophilic cytoplasm. A brisk mitotic activity was noted confirming the malignant nature of these cells. Although these islands of cells were present, the major part of the tumor was primarily like an abscess wall with necrosis and granulation tissue (Figure 2B, 2C, 2D). We performed periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) stains for fungal organisms, Zeehl-Neelson (ZN) stain for acid fast bacilli and gram's stain for bacteria. No organisms were identified. Meanwhile, pus sent for culture drew no growth and was sterile. Immunohistochemistry was performed with a panel of glial fibrillary acidic protein (GFAP) and pan-cytokeratin (CK) using using automated Ventana benchmark XT instrument. The tumor cells were positive for GFAP and negative for CK, confirming the glial nature of neoplastic cells (Figure 2E, 2F). It is worth noting that such growth pattern of neoplastic cells is reminiscent of a gliomatosis cerebri-like spread, although true

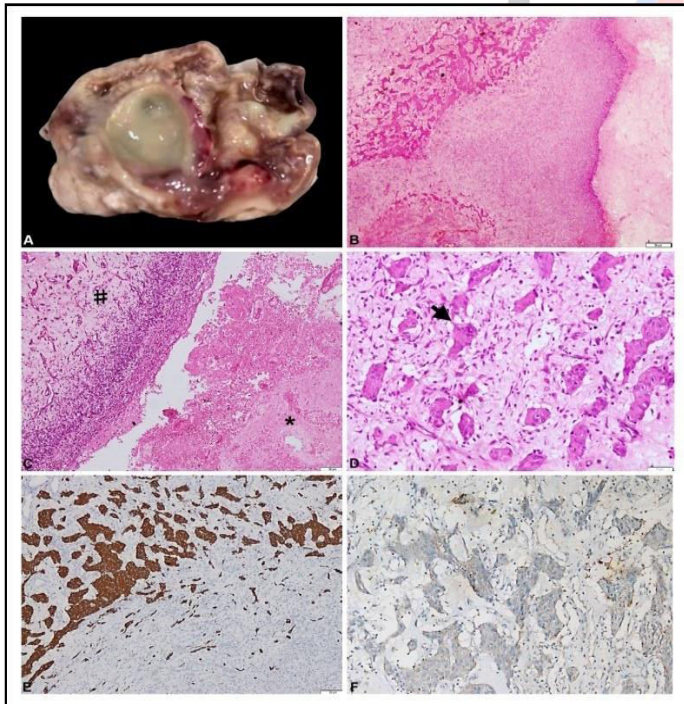


Figure 2. A well demarcated globular lesion is seen grossly with central necrosis and adjacent corrugated parenchyma (A). Photomicrographs showing

gliomatosis presents as diffuse hyperintensities on imaging rather than mass lesions. A final diagnosis of glioblastoma, WHO grade IV, not otherwise specified (NOS) was given.

The patient was treated with adjuvant radiotherapy, details of which were not available. However, on routine 3 month follow up the patient was doing well and no residual/recurrent lesion was noted on CT imaging (Figure 1B).

DISCUSSION:

Glioblastoma is the most common primary intracranial brain tumor in adults with an incidence rate of 3.16-3.21 per 100,000 which increases with age and reaching almost 17 per 100,000 person years by the age of 70 years [1, 2]. Despite advances in its standard of care, the prognosis of elderly GBMs remains dismal with a median survival ranging anywhere between 5 to 9 months [3,4,5].

Glioblastoma tends to arise in cerebral cortices as a rapidly enlarging mass lesion with a short duration of symptoms. The hallmark of tumor, i.e., microvascular proliferations of tumoral vessels along with neo-angiogenesis as a consequence of large vessel thrombosis provides leaky blood vessels which allow contrast dye to permeate it easily. This causes the radiological tumor margins to enhance in contrast displaying a ring-like enhancement. A similar mechanism occurs in infective abscesses and metastatic lesions of brain which are included in the radiological differential diagnoses in elderly patients especially in regions with high infection burden. MR spectroscopy has shown lactate and lipid peaks in both abscesses and tumors but only amino acid peaks (alanine, valine, leucine) in abscesses, although the authors considered it as soft distinguishing feature [6].

Another hallmark histological feature of glioblastoma is palisading necrosis which eventually breaks down to become confluent. It is now well understood, the mechanism by which glioma cells take hostage of host blood vessels and alter them for their survival

advantage. Chief mediators amongst those are VEGF/HIF- α axis, NF- κ B/AP-1/IL-8 pathway, mutated PTEN-Tissue factor response, PAR-1 upregulation and overexpression of HGF [7, 8]. These pathways working in tandem with other mediators like Ang-2 and TNF- α to damage the host blood vessels causing intra-luminal thrombosis [7]. This creates a hypoxic microenvironment around the damaged vessel culminating in necrosis which propagates centrifugally very rapidly. This hypoxic-necrotic environment has also been shown to impart pro-angiogenic, invasive and migratory properties to glioma cells lending the tumor its fatal reputation [8].

Unlike the necrosis induced by infectious agents, tumor necrosis in glioblastoma does not elicit any host response. Our case seems to be unusual in this aspect as a florid granulation tissue response was seen with an attempt to wall off the necrotic zone. A thorough examination of histology slides failed to detect any concomitant infectious agents responsible for such a response as reported rarely in the literature [9].

A metastatic squamous cell carcinoma of lung is also known to metastasize early with a predilection for cerebral cortex. Such lesions are also ring enhancing with a central area of necrosis and cystic degeneration. Similar to a glioblastoma, a host response is not known to occur.

CONCLUSION:

The case report gives an example of a rare pathological presentation of glioblastoma which might confuse the untrained eye and demonstrates the need for careful search for a neoplasm in such necrotic biopsy materials.

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